AMENDMENTS

IN THE SPECIFICATION

Please delete the paragraph beginning at page 12, line 9, and substitute the following amended paragraph.

-- Several species are particularly contemplated. For example, the invention provides a nucleic acid molecule wherein said Hu-Asp polypeptide is Hu-Asp1, and said polynucleotide molecule of (a) comprises the nucleotide sequence of SEQ ID NO.1; and a nucleic acid molecule wherein said Hu-Asp polypeptide is Hu-Asp2(a), and said polynucleotide molecule of (a) comprises the nucleotide sequence of SEQ ID NO. 3; and a nucleic acid molecule wherein said Hu-Asp polypeptide is Hu-Asp2(b), and said polynucleotide molecule of (a) comprises the nucleotide sequence of SEQ ID NO. 5. In addition to the foregoing, the invention provides an isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having the nucleotide sequence in (a) or (b) as described above. --

B1

Please delete the paragraph beginning at page 15, line 1, and substitute the following amended paragraph.

-- In one variation, the cells are collected and the critical peptide is the APP C-terminal peptide created as a result of the β secretase cleavage. In another variation, the supernatant is collected and the critical peptide is soluble APP, where the soluble APP has a C-terminus created by β secretase cleavage. In preferred embodiments, the cells contain any of the nucleic acids or polypeptides described above and the cells are shown to cleave the β secretase site of any peptide having the following peptide structure, P2, P1, P1', P2' (SEQ ID NO: 72), where P2 is K or N, where P1 is M or L, where P1' is D, where P2' is A. In one embodiment P2 is K and P1 is M and in another embodiment P2 is N and P1 is L. --

B2

Please delete the paragraph beginning at page 33, line 17, and substitute the following amended paragraph.

-- Figure 2: Figure 2 shows the nucleotide (SEQ ID NO: 5) and predicted amino acid sequence (SEQ ID NO: 6) of human Asp2(b). --

B3

Please delete the paragraph beginning at page 33, line 20, and substitute the following amended paragraph.

-- Figure 3: Figure 3 shows the nucleotide (SEQ ID NO: 3) and predicted amino acid sequence (SEQ ID NO: 4) of human Asp2(a). --

B4

Please delete the paragraph beginning at page 59, line 13, and substitute the following amended paragraph.

-- Several interesting features are present in the primary amino acid sequence of Hu-Asp2(a) (Figure 3 and SEQ ID No. 4) and Hu-Asp-2(b) (Figure 2, SEQ ID No. 6). Both sequences contain a signal peptide (residues 1-21 in SEQ ID No. 4 and SEQ ID No. 6), a pro-segment, and a catalytic domain containing two copies of the aspartyl protease active site motif (DTG/DSG). The spacing between the first and second active site motifs is variable due to the 25 amino acid residue deletion in Hu-Asp-2(b) and consists of 168-versus-194 amino acid residues, for Hu-Asp2(b) and Hu-Asp-2(a), respectively. More interestingly, both sequences contains a predicted transmembrane domain (residues 455-477 in SEQ ID No.4 and 430-452 in SEQ ID No. 6) near their C-termini which indicates that the protease is anchored in the membrane. This feature is not found in any other aspartyl protease except Hu-Asp1. --

B5

IN THE SEQUENCE LISTING:

Please replace the substitute sequence filed on April 30, 2001 (pages 1-67) with the second substitute sequence listing (pages 1-92) submitted herewith.

IN THE CLAIMS

Please renumber claims 65-68 (as originally presented) as claims 64-67, respectively; please renumber the first claim 69 (as originally presented) as claim 68; and please amend renumbered claim 67 and claim 70 as follows. (Please cancel any claim renumbering by the Patent Office that is inconsistent with these changes.)

64. (Amended) A method of claim 53, wherein the detectable label is selected from the group consisting of radioactive labels, enzymatic labels and flourescent labels.

B7

65. (Amended) A method of claim 53, wherein the APP substrate comprises a human APP isoform and further comprises a carboxy-terminal di-lysine.